UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/654,743	09/01/2000	Robert G. Korneluk	07891/003005	7148

7590 05/08/2003

Kristina Bieker-Brady, Ph.D.
Clark & Elbing LLP
176 Federal Street
Boston, MA 02110

EXAMINER
KAUSHAL, SUMESH

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 05/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/654,743	KORNELUK ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 3-14, 30-32, 48-78* is/are pending in the application.

4a) Of the above claim(s) *1,3-14,30-32,48,49 and 51-78* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *01 September 2000* is: a)☐ approved b)☒* disapproved by the Examine

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)*
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's response filed on 02/12/03 has been acknowledged.

Election/Restrictions

Applicant's election without traverse of Group VII claim 50 (SEQ ID NO:47) in Paper No. 7 is acknowledged. The applicant further elected nucleotide sequences of SEQ ID NO:47 (human BIR III). Furthermore, in response to applicants arguments filed on paper NO:7 human and mouse nucleotide sequences which represent XIAP BIRIII domain (SEQ ID NO: 47 and 51) has been examined in this office action.

The applicant argues that it would impose no undue burden to search six human and mouse nucleic acid encoding XIAP BIR domains (SEQ ID NO: 45, 46, 47, 49, 50 and 51). This is not found persuasive since each SEQ ID NO as claimed represents structurally and functionally distinct BIR domains, wherein the search of one is not required for other. Furthermore search of a particular SEQ ID NO would not lead to finding other, since nucleic acid encoding BIRI, BIRII and BIRIII are structurally distinct nucleotide sequences. In addition each BIR domain has been characterized by a functionally distinct IAP (inhibition of apoptosis activity), which involves different caspases. Thus there is a serious burden to examine the proposed nucleotide sequences in one single invention. The requirement is deemed proper and is therefore made FINAL.

Claims 1, 3-14, 30-32, 48-49 and 51-78 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 7.

Claim 50 is examined in this office action.

*Applicants are advised to follow Amendment Practice under revised 37 CFR 1.121 (http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/revamdtprac.htm). Each amendment document that includes a change to an existing claim, or submission of a new claim, **must include a complete listing of all claims** in the application. After each claim number, the status must be indicated in a parenthetical expression, and the text of each claim under examination (with markings to show current changes) must be presented. The listing will serve to replace all prior versions of the claims in the application.*

Claim Objections

1. Claim 50 is objected to because of the following informalities: Instant claim is objected to because it encompasses non-elected subject matter (SEQ ID NO: 45-46, 49-50, 53-55, 57-59, 61-63 and 65-67), wherein the elected subject matter is SEQ ID NO:47 and 51 (xiap BIRIII domain). Appropriate correction is required.

Double Patenting

3. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claim 50 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 7 of prior U.S. Patent No. 6156535. This is a double patenting rejection.

Claim 7 of the U.S. Patent No. 6156535 claims "A substantially pure nucleic acid encoding a baculovirus inhibitor of apoptosis repeat (BIR) domain, said nucleic acid comprising a sequence selected from the group consisting of SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 47, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 53, SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 65, SEQ ID NO: 66, and SEQ ID NO: 67" subject matter of which is identical to the invention as claimed in the claim 50 of instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 50 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, **had possession of the claimed invention.**

The scope of instant invention as claimed encompasses a nucleic acid sequence encoding a baculovirus inhibitor of apoptosis (BIR) domain wherein the nucleic acid comprises a sequence selected from the group consisting of SEQ ID NO: 47 and 51. Given the broadest reasonable interpretation scope of invention as claimed encompasses a nucleotide sequence, which encodes any and all BIR domains (in any and structural organization), in addition to nucleic acid sequence of SEQ ID NO:47 or 51. In addition the scope of instant invention encompasses a nucleic acid (as claimed) obtained from any and all organisms. At best the specification as filed only teaches human and mouse XIAP polypeptide which comprises BIR III domain encoded by the nucleotide sequences of SEQ ID NO: 47 and 51 (spec. page 19 table-1). Besides human and mouse xiap and hiap sequences, which comprises BIRIII domain the instant specification fails to disclose any other nucleic acid sequences that encodes a BIR domain (other than BIRI, BIR II or BIRIII) in addition to the nucleic acid sequence of SEQ ID NO: 47 and 51. Clearly the scope of invention as claimed encompasses an IAP-like polypeptide wherein one of BIR domain comprises the nucleotide sequence of SEQ ID NO: 47 and 51.

Applicant is referred to the Interim guidelines on ***Written Description*** published December 21, 1999 in the Federal Register, Vol. 64, No. 244, pp. 71427-71440. The disclosure

of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see In re Shokal 113USPQ283(CCPA1957); Purdue Pharma L. P. vs Faulding Inc. 56 USPQ2nd 1481 (CAFC 2000). In instant case the scope of the nucleic acid sequence as claimed encompasses a genus of inhibitor of apoptosis proteins (IAP) wherein the protein has been identified only by means single BIR domain represented by SEQ ID NO:47 or 51. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USP2d 1481 at 1483. In Fiddes, claims directed to a mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Similarly, in the instant case the instant specification only discloses mouse and human XIAP sequences comprising the nucleotide sequence of SEQ ID NO:47 and 51 respectively.

*Furthermore the specification defines that: by "**BIR domain**" is meant a domain having the amino acid sequence of the consensus sequence: Xaa1 Xaa1 Xaa1 **Arg Leu** Xaa1 **Thr Phe** Xaa1 Xaa1 **Trp Pro** Xaa2 Xaa1 Xaa1 Xaa2 Xaa2 Xaa1 Xaa1 Xaa1 Xaa1 **Leu Ala** Xaa1 **Ala Gly Phe Tyr Tyr** Xaa1 **Gly** Xaa1 Xaa1 **Asp** Xaa1 **Val** Xaa1 **Cys Phe** Xaa1 **Cys** Xaa1 Xaa1 Xaa1 Xaa1 Xaa1 Xaa1 **Trp** Xaa1 Xaa1 Xaa1 **Asp** Xaa1 Xaa1 Xaa1 Xaa1 Xaa1 **His** Xaa1 Xaa1 Xaa1 Xaa1 **Pro** Xaa1 **Cys** Xaa1 **Phe Val**, wherein Xaa1 is any amino acid and Xaa2 is any amino acid or is absent (SEQ ID NO:2) see spec page 11, line 29.*

Accordingly the BIR domain as defined by the instant specification requires only 32% amino acid sequence conservation wherein 68% of the amino acid sequences varies in any and all fashion. It is general knowledge in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. The nucleic acid sequences as claimed are mere hypothetical sequences because no biological function has been established for other than the disclosed human and mouse xiap proteins. The mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues. see Ngo, in The Protein Folding Problem and Tertiary Structure Prediction, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and

492-495, 1994). Rudinger (in Peptide Hormones, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976). Therefore the applicant has not disclosed the invention as claimed.

In addition the possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *See, e.g., Pfaff v. WellsElectronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).* In claims to genetic material, generic statement such as "vertebrate insulin cDNA" or mammalian insulin cDNA," without more, is not adequate written description of claimed genus, since it does not distinguish genus from others except by function, and does not specifically define any of genes that fall within its definition, or describe structural features commonly possessed by members of genus that distinguish them from others; accordingly, naming type of material generally known to exist, in absence of knowledge as to what that material consists of, is not description of that material (*Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406).*

In instant case the nucleic acid sequence as claimed has been defined by presence of any and all baculovirus inhibitor of apoptosis repeat domains (other than BIRI, BIRII or BIRIII) in addition to the of nucleotides of SEQ ID NO:47 and 51. The instant specification defines BIR domain that encompasses at least 68% amino acid sequences variation (supra). The invention as claimed has been defined only by a statement of function that broadly encompasses inhibition of apoptosis or BIR domain-related activity, which conveyed no distinguishing information about the identity of the claimed DNA sequence, such as its relevant structural or physical characteristics. According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim.

5. Claim 50 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid sequence encoding a BIR domain wherein the BIR domain comprises a nucleic acid sequence selected from the group consisting of SEQ ID NO: 47 and 51, does not reasonably provide enablement for any and all nucleic acid sequence encoding any and all BIR domains wherein the nucleic acid comprises a sequence selected from group consisting of SEQ ID NO:47 and 51. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention **commensurate in scope** with these claims.

Nature Of Invention:

The invention relates to nucleic acid sequence encoding an IAP-like protein (inhibitor of apoptosis protein) that comprises BIR domains.

Breadth Of Claims And Guidance Provided By The Inventor:

The scope of invention as claimed encompasses a nucleic acid sequence isolated from any and all organism that encodes a IAP-like protein comprising an undefined BIR domain and a XIAP BIRIII domain consisting of SEQ ID NO: 47 and 51. Clearly the invention as claimed reads upon a nucleotide sequence that encodes a xiap-like polypeptide. At best the specification as filed teaches human and mouse XIAP polypeptides which comprises the nucleotide sequences of SEQ ID NO: 47 and 51 (spec. page 19 table-1). Besides human and mouse xiap and hiap sequences, which comprises BIRIII domain the instant specification fails to disclose any other nucleic acid sequences that encodes any BIR domain in addition to the nucleic acid sequence of SEQ ID NO: 47 and 51 and have IAP (inhibitor of apoptosis protein)-like activity..

State Of Art And Predictability:

Members of the IAP (inhibitor of apoptosis) family of proteins are found in all animals and regulate apoptosis in large part by binding and inhibiting the caspase proteases required for apoptosis. Members of the IAP family include human **XIAP, NAIP, and survivin, *Drosophila* DIAP1, and baculovirus *Orgyia pseudotsugata* Op-IAP**. Genes for IAPs have been identified in insects, birds, fish, mammals, and 19 different viruses. IAPs contain one, two, or three repeats of a conserved 65-residue sequence called the BIR (baculovirus inhibitor of apoptosis repeat) motif which is required for stimulator binding and for stimulator regulation of IAP-caspase inhibition. Even though BIR domain is integral to the stimulator activation of IAP-bound

caspases, the activation of IAP-bound caspases varies type of BIR domain. For example in the BIR3 of XIAP, the BIR surface groove binds caspase-9, so that Smac-BIR3 association competitively dissociates and activates caspase-9. In BIR2 of XIAP, Smac association activates caspase-3 and caspase-7 molecules bound to residues adjacent to the BIR domain (Luque et al, *Biochemistry,* **41**(46): 13663 -13671, 2002, see page 13663). The instant specification defines BIR domain as a domain wherein at least 68% of amino acid sequence in a 68 amino acid long domain varies in any and all fashion (supra). It is general knowledge in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. The recited nucleic acid sequences as claimed are mere hypothetical sequences because no biological function has been established for other than the disclosed human and mouse xiap proteins. The mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues. see Ngo, in The Protein Folding Problem and Tertiary Structure Prediction, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and 492-495, 1994). Rudinger (in Peptide Hormones, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976). Therefore the applicant has not presented enablement commensurate in scope with the claims.

Quantity Of Experimentation Required:

In instant case screening of any and all natural and/or non-natural nucleotide sequences for an IAP-like activity wherein the nucleotide comprise any BIR domain in addition to the nucleotide sequences of SEQ ID NO:47 and 51 is not considered routine in the art. Furthermore making and testing a polypeptide comprising a BIR domain other than BIRI, BIRII or BIRIII domain, wherein 68% amino acids are added, deleted and/or substituted is significantly different from the making and testing a polypeptide that comprises amino acid sequences identical to known BIR domains. The number of possible scenario increase geometrically with increase in percent non-identity. Such making and testing is nothing more than an invitation to further experimentation, since the specification can not be relied on to teach how to make the variants as claimed. One has to engage in extensive making and testing in order to obtain variants that meet

the requirements for the claimed IAP activity. This is not considered routine in the art and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed. Thus, the applicant has not presented enablement commensurate in scope with the claims.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 703-305-6838. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-8724 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

S. Kaushal
PATENT EXAMINER

SUMESH KAUSHAL
PATENT EXAMINER

REMY YUCEL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

John J. Doll, Director
Technology Center 1600